

Botulinum toxin A improves involuntary limb movements in Rasmussen syndrome

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Rasmussen syndrome (RS) is a focal, progressive, cortical inflammation affecting one cerebral hemisphere that usually presents with epilepsy partialis continua (EPC) that is resistant to antiepileptic drugs (AEDs). The encephalitis is often associated with ipsilateral cerebral hemisphere and basal ganglia atrophy.¹ Patients can develop involuntary movements, including myoclonus, dystonia, and athetosis, usually in association with EPC.² The encephalitis is probably autoimmune mediated, although the pathogenesis of the atrophy is unknown.³ We report a man with established RS who developed EPC and painful dystonia that improved with botulinum toxin A (BTX-A).

Case report. We described previously this 43-year-old, left-handed man.⁴ He sought treatment in 1989 for EPC followed by neurologic and cognitive deficits. The following therapies had no sustained effect: multiple AEDs, right corticectomy in 1990, infusions of sodium valproate or benzodiazepines into the corticectomy cavity in 1994, and right frontoparietal subcortical transection in 1995. Immunomodulatory therapy started in 1996, and his condi-

tion improved, although he continued to have intermittent bouts of left upper limb myoclonic jerking.⁴

He was stable until 2002 when he had several *Klebsiella pneumoniae* bacteremias. Frequent complex partial seizures (CPSs) developed, and EPC returned with continuous myoclonic jerking of the left upper limb and frequent, painful, dystonic, flexor spasms of the left fingers, wrist, and elbow, which sometimes spread to the shoulder. Although the CPS remitted with IV antibiotics and increasing his AED regimen (topiramate, 800 mg/d; phenytoin, 425 mg/d; levetiracetam, 3 g/d; and vigabatrin, 2 g/d), his involuntary movements persisted. Clonazepam (20 mg/d), IV midazolam boluses, and increasing prednisolone (1.5 mg/kg/d) and IV immunoglobulin (hIVIg; 2 g/kg fortnightly) doses had no effect. There was progressive atrophy of the remaining right cerebral hemisphere, caudate nucleus, and thalamus on serial brain MRI scans since 1993 (figure). However, there was no evidence of reactivation of brain inflammation on either the MRI scans or serial CSF analysis.

We tried freehand injections of BTX-A (Dysport, Ipsen, UK; total dose, 1000 mouse units [MU]) into the most affected left upper limb muscles (200 MU into biceps and flexor digitorum superficialis; 100 MU into trapezius, brachioradialis, triceps, flexor carpi radialis, and flexor digitorum profundus; and 50 MU into flexor carpi ulnaris and the thenar muscles). Marked im-

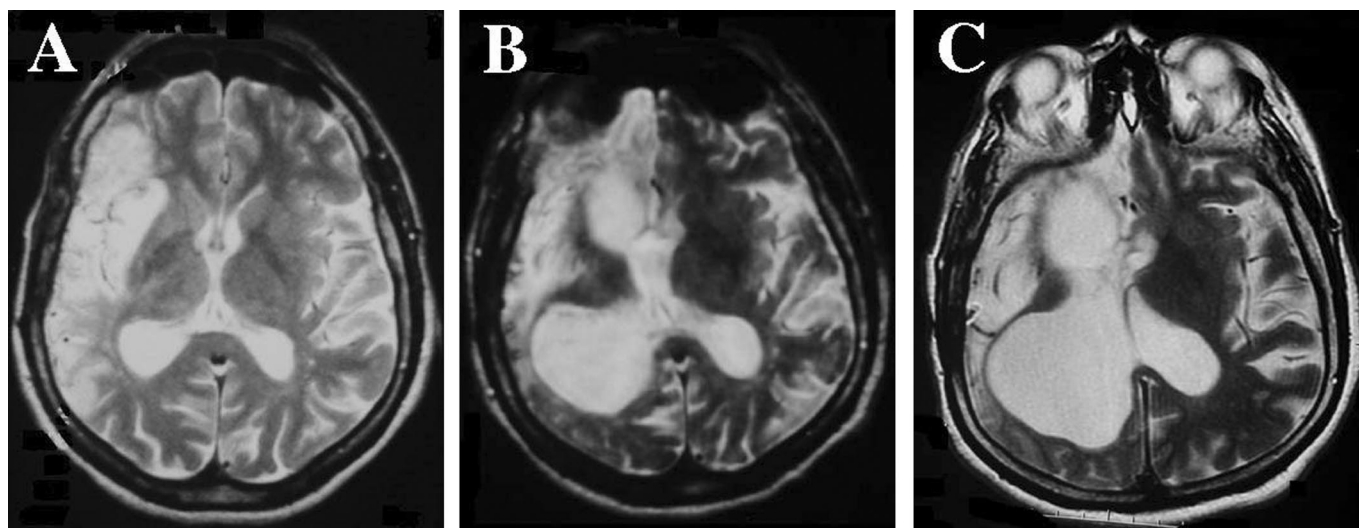


Figure. Progressive right basal ganglia and thalamic atrophy on serial MRI brain scans in a man with Rasmussen syndrome. (A) MRI brain scan in 1993, 3 years after right central sulcus lesionectomy. There is extensive high T2-weighted signal in the right hemisphere and normal basal ganglia and thalamus. (B) MRI brain scan in 1996 just before the start of immunomodulatory treatment. There is marked right hemisphere and basal ganglia atrophy. (C) MRI brain scan in 2002 at the onset of left upper limb myoclonus and dystonia. Right hemisphere and basal ganglia atrophy has progressed.

provement of his involuntary movements began 1 week later. His painful spasms resolved over 2 weeks; the jerking became intermittent; and useful limb function returned. His dose of topiramate was reduced to 400 mg/d; phenytoin was reduced to 350 mg/d; vigabatrin was reduced to 750 mg/d; and clonazepam was reduced to 2 mg/d. After 5 months, his involuntary movements reappeared. Additional BTX-A injections into the affected muscles (total dose, 500 MU) reproduced the effects of the first treatment.

Discussion. Repeated BTX-A injections were an effective treatment for our patient's late-onset, limb dystonia and continuous myoclonic jerking. Changes in the ipsilateral basal ganglia in association with cerebral hemisphere abnormalities are common in patients with RS and usually appear early in the course of the syndrome. In one serial MRI study, eight of eight patients with RS had atrophy of the head of the caudate nucleus at 4 months after onset of symptoms.¹ In another patient, atrophy of the right caudate, globus pallidus, and putamen and mild increased T2-weighted signal in the right striatum were the only MRI brain scan findings at presentation.⁵ However, no additional EPC-associated involuntary movements were described in any of these patients, and reports of hyperkinetic movements other than myoclonus are rare in EPC associated with RS.² When these movements occur, they start typically at the onset or early in the course of the syndrome.² By contrast, our patient's involuntary movements started 14 years after the clinical onset of RS when there was established caudate atrophy. Human IVIg improved athetosis, dystonia, and EPC in one woman with RS, although the response was short lasting.² Increasing the doses of prednisolone and hIVIg had no effect on our patient's involuntary movements.

Our patient's repeated response to BTX-A contrasts with the reports of its ineffectiveness in two patients with EPC and in two children with RS and EPC.^{6,7} These previous findings suggest that uncomplicated EPC may be resistant to this therapy. However, it can be difficult clinically to distinguish the recurrent, simple focal

motor seizures of EPC from the other hyperkinetic movements, especially myoclonus, occurring in patients with established RS.

We propose that BTX-A can be a useful, long-term therapy for involuntary, hyperkinetic movements in RS and that it should be considered especially for those patients with late-onset, focal movements that do not respond to conventional AED treatment or immunotherapy.

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